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AF 1644

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Wouters et al.

Serial No.: 09/780,205

Filed: February 9, 2001

For: ANTIBODIES FOR USE IN TARGETED AND TEMPORARY TREATMENT OF HUMANS AND ANIMALS

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APPEAL BRIEF

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Commissioner for Patents
P.O. Box 1450
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Attn: Board of Patent Appeals and Interferences

Sir:

This brief is submitted in accordance with the Requirements of 37 C.F.R. § 41.37(c), and along with the fee set forth in 37 C.F.R. § 41.20(b)(2).

REAL PARTY IN INTEREST

The real parties of interest are Stanislaus Wouters, Heinz Renggli, and Danielle Horbach, the inventors of the pending application.

RELATED APPEALS AND INTERFERENCES

None of the appellants or the appellants' representatives are aware of any pending appeal or interference which would directly affect, be directly affected by, or have any bearing on the Board's decision in the present pending appeal.

STATUS OF CLAIMS

Claims 1, 3-8, 11-12, 32-34, 36-39 and 41 have been canceled from the application.

Claims 2, 9-10, 13-22, 24, 27-31, 35, 40 and 42-49 are currently pending in the application and stand rejected.

Claims 23, 25 and 26 are withdrawn as being directed to a non-elected invention.

No claims are allowed.

The rejection of claims 2, 9-10, 13-22, 24, 27-31, 35, 40 and 42-49 is being appealed.

STATUS OF AMENDMENTS

The appellants filed an Amendment under 37 C.F.R. § 1.116 on October 8, 2004. The Examiner entered the amendments as indicated in the Advisory Action of November 4, 2004.

No other amendments to the claims have been filed.

SUMMARY OF CLAIMED SUBJECT MATTER

Independent claim 40 relates to a selected monoclonal antibody, or fragment thereof. (*See*, Specification as-filed, page 2, line 21). The selected monoclonal antibody, or fragment thereof, has been selected for its ability to bind to an epitope at a first pH of 8.5. (*See*, *Id.* at page 2, lines 22-23 and page 7, lines 5-6). The selected monoclonal antibody, or fragment thereof, has also been selected such that the bond of the selected monoclonal antibody, or fragment thereof, to the epitope is broken at a second pH of 7. (*See*, *Id.* at page 2, lines 23-24 and page 7, line 5).

Independent claim 42 is directed towards a selected monoclonal antibody, or fragment thereof. (*See, Id.* at page 2, line 21). The selected monoclonal antibody, or fragment thereof, has been selected for its ability to bind an epitope at a first pH of 8.5. (*See, Id.* at page 2, lines 22-23 and page 7, lines 5-6). The selected monoclonal antibody, or fragment thereof, has also been selected such that the bond of the selected monoclonal antibody, or fragment thereof, to the epitope is broken at a second pH of 4.5 and an ion strength of 1M NaCl. (*See, Id.* at page 2, lines 23-24 and page 7, line 6).

The selected monoclonal antibodies or fragments thereof of claims 40 and 42 have utility in being able to target diagnostically, therapeutically and cosmetically active substances to desired epitopes, wherein the selected monoclonal antibodies or fragments thereof may be removed from the epitope at a desired moment. (*See, Id.* at page 1, lines 6-10 and page 2, lines 27-33).

GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

I. Whether claims 2, 9, 10, 13-22, 24, 27-31, 35, 40 and 42-49 lack enablement under 35 U.S.C. § 112, first paragraph?

II. Whether claims 2, 9, 10, 13-22, 28, 30-31, 35, 40 and 42-49 are unpatentable under 35 U.S.C. § 103(a) over Beggs et al. (U.S. Pat. 5,490,988) in view of Goding ("Production and Application of Monoclonal Antibodies in Cell Biology, Biochemistry and Immunology," MONOCLONAL ANTIBODIES: PRINCIPLES AND PRACTICE, Academic Press, 1986)?

III. Whether claims 2, 9, 10, 13-21, 24, 27, 28, 30, 31, 35, 40 and 42-49 are unpatentable under 35 U.S.C. § 103(a) over Cummins et al. (EP 0736544A1) in view of Goding?

IV. Whether claim 29 is unpatentable under 35 U.S.C. § 103(a) over Beggs et al. in view of Goding, and further in view of Cole et al. ("Humoral Immunity to Commensal Oral Bacteria: Avidity of Serum IgG and IgM Antibodies Reactive with *Porphyromonas* (*Bacteroides*) *Gingavalis* in Children," *Immun. & Infect. Diseases*, Vol. 3, pp. 33-35 (1993))?

V. Whether claim 43 is unpatentable under 35 U.S.C. § 103(a) over Beggs et al. in view of Goding, and further in view of Fischer (U.S. Patent 5,571,511)?

ANALYSIS/ARGUMENT

Rejections under 35 U.S.C. 112, first paragraph

Claims 2, 9, 10, 13-22, 24, 27-31, 35, 40 and 42-49 stand rejected under 35 U.S.C. § 112, first paragraph, as assertedly lacking enablement.

The Final Office Action asserted that the specification is only "enabling for an antibody or fragment thereof and composition comprising said antibody or fragments which binds to an epitope and broken from an epitope under specifically chosen conditions recited in Table 1." (Final Office Action, page 2). In the Advisory Action, the examiner asserted that "the specification, while being enabling for an antibody or fragment thereof and composition comprising said antibody or fragments which binds to an epitope and broken from an epitope under specifically chosen conditions recited in Table 1 that binds to a dye and detects the plaque and suitable for detection of dental plaque or other oral pathogens." (Advisory Action, page 3).

The standard for determining whether a claim is enabled by an application is "whether that disclosure, when filed, contained sufficient information regarding the subject matter of the claims as to enable one skilled in the pertinent art to make and use the claimed invention" without undue experimentation. (M.P.E.P. § 2164.01). In the case of *In re Wands*, the Federal Circuit laid out factors to be considered in determining whether sufficient evidence exists to establish enablement. (*See, In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988)).

In re Wands is particularly instructive to the instant case on appeal since the instant case is directed towards selected monoclonal antibodies and the claims at issue in *In re Wands* were directed towards an immunoassay method using a monoclonal high affinity IgM antibody having a specific binding affinity constant for HBsAg determinants. (*See, In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404).

The Federal Circuit indicated that "[t]he sole issue is whether, in this particular case, it would require undue experimentation to produce high-affinity IgM monoclonal antibodies. Enablement is not precluded by the necessity for some experimentation such as routine screening." (*Id.* at 1404). The Federal Circuit stated that the factors to be considered in determining whether a disclosure would require undue experimentation include

> (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the

> nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

(*Id.* at 1404).

In considering these factors, the Federal Circuit indicated that "it is necessary to discuss further the methods for making specific monoclonal antibodies." (*Id.*) In the instant appeal, the appellants' specification provides considerable direction and guidance on how to make and use the antibodies or fragments thereof of claims 2, 9, 10, 13-22, 24, 27-31, 35, 40, and 42-49.

For instance, Example 1 of the as-filed specification outlines how to obtain monoclonal phage-antibody fragments particles from a phage library, and how to screen for the monoclonal phage-antibody fragments that possess the binding characteristics of the selected monoclonal antibodies or fragments thereof of claims 2, 9, 10, 13-22, 24, 27-31, 35, 40 and 42-49. (*See*, Specification at page 6, line 3 through page 11, line 24). Example 1 further indicates that helper phages were added to *E. coli* bacteria in order to form the monoclonal antibodies or fragments thereof (*i.e.*, the phages). (*See*, Specification as-filed, page 6, lines 10-15). The precipitated monoclonal antibodies or fragments thereof were placed in various binding buffers with the epitope (*i.e.*, *S. epidermidis*) and washed 12 times. (*See*, *Id.* at lines 18-29). The monoclonal antibodies or fragments thereof that remained bound to the epitope were eluted from the epitope, and subjected to another round of selection in order to select for the monoclonal antibodies or fragments thereof. (*See*, *Id.* at lines 29-35). Thus, the as-filed specification provides considerable direction and guidance on how to make and use the selected monoclonal antibodies or fragments thereof.

With regard to the factors of the nature of the invention, the state of the prior art and the relative skill of those in the art, since the instant case and the *In re Wands* case both deal with monoclonal antibodies, the Federal Circuit's statement that "there was a high level of skill in the art at the time when the application was filed, and all of the methods needed to practice the invention were well known" is also applicable to the instant case on appeal. (*In re Wands* at 1406).

Another factor is the presence of absence of working examples. In formulating the enablement rejection, the examiner stated "[a]pplicant himself acknowledge [sic] that the

specification disclosed only 16 specific clones out of the entire phage display library, which includes, at the very least, millions of candidate monoclonal antibodies, that possess the required specific characteristics as recited in Table 1." (Final Office Action at page 3). However, the Federal Circuit indicated that "it seems unlikely that undue experimentation would be defined in terms of the number of hybridomas that were never screened. Furthermore, in the monoclonal antibody art it appears that an 'experiment' is not simply the screening of a single hybridoma, but is rather the entire attempt to make a monoclonal antibody against a particular antigen." (*In re Wands* at 1406-07). Thus, the examiner's conclusion that only a certain number of clones worked and that other candidate antibodies **may** exist that possess the claimed characteristics cannot negate enablement. For instance, the *In re Wands* case indicated that enablement existed when only four hybridomas were disclosed to produce antibodies within the scope of the claims. (*See, Id.* at 1405). Thus, one of ordinary skill in the art would be able to make and use the subject matter of claims 2, 9, 10, 13-22, 24, 27-31, 35, 40 and 42-49 without undue experimentation.

Claim 40

Independent claim 40 is directed to a selected monoclonal antibody, or fragment thereof, that has been selected for its ability to bind to an epitope at a first pH of 8.5 and such that the bond of the selected monoclonal antibody, or fragment thereof, to the epitope is broken at a second pH of 7.

The as-filed specification discloses a working example of a selected monoclonal antibody or fragment thereof having the binding characteristics recited in claim 40. For instance, Table 4 of the as-filed specification indicates that clone 3 is able to bind to and disassociate from an epitope under the selection conditions of B, C and D of Table 1. (*See*, Specification as-filed, Table 4, page 11). Table 1 of the as-filed specification indicates that condition C has binding conditions of a pH of 8.5 and elution conditions of a pH of 7 (*e.g.*, Milli Q water), and condition D has binding conditions of a pH of 8.5. (*See, Id.* at Table 1, page 7). Since clone 3 was selected under both conditions C and D, both having a binding pH of 8.5 and wherein condition C has an elution condition of a pH of 7, the binding and elution conditions of the antibody or fragment thereof of claim 40 are specifically enabled by the as-filed specification.

Since the as-filed specification discloses a working example of the antibody, or fragment thereof, of claim 40, one of ordinary skill in the art would be able to make and use the selected monoclonal antibody, or fragment thereof, of claim 40 without undue experimentation. Withdrawal of the enablement rejection of claim 40 is requested.

Claim 43

Claim 43 depends from independent claim 40 and indicates that the epitope is of a *Staphylococcus epidermidis* origin. Claim 43 should be enabled for the same reasons as base claim 40 and since the as-filed specification indicates that the epitope to which the selected monoclonal antibody or fragment thereof of claim 40 binds is *S. epidermidis*. (*See*, Specification as-filed at page 6, line 25).

Claim 2

Claim 2 depends from claim 40 and indicates that the selected monoclonal antibody or fragment thereof is coupled to a diagnostically, therapeutically or cosmetically active substance. Claim 2 should be enabled for the same reasons as base claim 40 and since the as-filed specification teaches that the diagnostically, therapeutically or cosmetically active substance can be coupled to the selected monoclonal antibody or fragment thereof as described in EP 0453097, EP 0451972 and EP 0450800, or as according to Lal et al. (Immunol. Meth. 1985; 79:307-318), and that such substance may be enzymes, dyes, fluorescent substances, radioactive substances or antimicrobial compounds. (*See*, *Id.* at page 4, lines 1-8). As stated in the MPEP, "the test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation... A patent need not teach, and preferably omits, what is well known in the art." (M.P.E.P. § 2164.01, *citing United States v. Telectronics, Inc.*, 857 F2d 778, 785, 8 USPQ 2d 1217, 1223 (Fed. Cir. 1988) and *In re Buchner*, 929 F2d 660, 661, 18 USPQ2d 11331, 1332 (Fed. Cir. 1991). Thus, since the as-filed specification discloses how to make the selected monoclonal antibody or fragment thereof, one of ordinary skill in the art would be able to couple the selected monoclonal antibody or fragment thereof to the diagnostically, therapeutically or cosmetically active substance using the information known in the art.

The as-filed specification further discloses a working example of a diagnostically, therapeutically or cosmetically active substance (*i.e.*, erythrocin) that was bound to the selected monoclonal antibody or fragment thereof, wherein the selected monoclonal antibody or fragment thereof coupled to the diagnostically, therapeutically or cosmetically active substance exhibited the binding characteristics of claim 40. (*See, Id.* at page 11, lines 27-36).

Claim 9

Claim 9 depends from claim 40 and indicates that the ability of the selected monoclonal antibody or fragment thereof to bind to the epitope has been further selected dependent upon ion strength. Claim 9 should be enabled for the same reasons as base claim 40 and since the as-filed specification describes conditions for binding the selected monoclonal antibody or fragment thereof include ion strength. (*See, Id.* at page 3, lines 20-21). The as-filed specification further describes a working example of a selected monoclonal antibody or fragment thereof that binds to an epitope at an ion strength (*i.e.*, about 1M NaCl). (*See, Id.* at Table 1, page 7).

Claim 10

Claim 10 depends from claim 9 and indicates that a first ion strength at which the selected monoclonal antibody binds the epitope is different that a second ion strength at which the bond between the selected monoclonal antibody and the epitope is broken. Claim 10 should be enabled for the same reasons as base claim 40 and since the as-filed specification describes a working example of a selected monoclonal antibody that binds to an epitope at a first ion strength (*i.e.*, 1M NaCl), wherein the bond between the selected monoclonal antibody and the epitope is broken at a second ion strength (*i.e.*, Milli Q water).

Claim 13

Claim 13 depends from claim 40 and indicates that the selected monoclonal antibody or fragment thereof is selected from a group consisting of F(ab), F(ab)', $F(ab)'_2$ and an scFv. Claim 13 should be enabled for the same reasons as base claim 40 and since the as-filed specification indicates that the selected monoclonal antibody or fragment thereof are selected from a phage library of Fab fragments or single chain Fv libraries. (*See, Id.* at page 3, lines 11-13 and lines 37-38). The as-filed specification also describes a working example of a selected monoclonal

antibody or fragment thereof selected from a human Fab phage library. (*See, Id.* at page 6, line 9).

Claim 14

Claim 14 depends from claim 40 and indicates that the selected monoclonal antibody or fragment thereof is capable of use in a targeted or temporary diagnostic, therapeutic and cosmetic treatment of externally accessible parts of the human or the animal body. Claim 14 should be enabled for the same reasons as base claim 40 and since the as-filed specification discloses that the antibodies or fragments thereof may be used for the treatment of externally accessible parts of the human body, and further discloses a working example of a selected monoclonal antibody or fragment thereof that is incorporated into toothpaste. (*See, Id.* at page 4, lines 16-20 and page 11, lines 25-36).

Claim 15

Claim 15 depends from claim 14 and indicates that the targeted or temporary diagnostic, therapeutic or cosmetic treatment comprises a treatment of an oral cavity of the human or the animal body. Claim 15 should be enabled for the same reasons as base claim 40 and since the as-filed specification discloses a working example of incorporating the selected monoclonal antibody or fragment thereof in toothpaste and treating an oral cavity with the toothpaste. (*See, Id.* page 11, lines 25-36).

Claim 16

Claim 16 depends from claim 15 and indicates that the selected monoclonal antibody or fragment thereof is capable of bleaching teeth and molars in the oral cavity. Claim 16 should be enabled for the same reasons as base claim 40 and since the as-filed specification discloses that a bleaching agent can be coupled to the selected monoclonal antibody or fragment thereof and be used to treat the oral cavity. (*See, Id.* at page 4, lines 1-15).

Claim 17

Claim 17 depends from claim 15 and indicates that the selected monoclonal antibody or fragment thereof is capable of detecting plaque in the oral cavity. Claim 17 should be enabled for the same reasons as base claim 40 and since the as-filed specification discloses that the selected monoclonal antibody or fragment thereof can be selected to bind to a microbial species in the oral microflora that forms plaque. (*See, Id.* at page 4, lines 21-31).

Claim 18

Claim 18 depends from claim 15 and indicates that the selected monoclonal antibody or fragment thereof is capable of removing plaque in the oral cavity. Claim 18 should be enabled for the same reasons as base claim 40 and since the as-filed specification indicates that an antimicrobial substance can be coupled to the selected monoclonal antibody or fragment thereof, wherein the selected monoclonal antibody or fragment thereof is able to target the antimicrobial substance and attach to the microbes that form plaque. (*See, Id.* at page 4, lines 30-35).

Claim 19

Claim 19 depends from claim 14 and indicates that the targeted or temporary diagnostic, therapeutic or cosmetic treatment comprises a treatment for fighting infections in externally accessible parts of the human of the animal body. Claim 19 should be enabled for the same reasons as base claim 40 and since the as-filed specification indicates that the selected monoclonal antibody or fragment thereof can be coupled to an antimicrobial compound and used to treat infections in externally accessible parts of the human or animal body. (*See, Id.* at page 4, lines 1-15).

Claim 20

Claim 20 depends from claim 2 and indicates that the diagnostically, therapeutically or cosmetically active substance comprises an enzyme. Claim 20 should be enabled for the same reasons as base claim 40 and since the as-filed specification discloses an enzyme as the diagnostically, therapeutically or cosmetically active substance. (*See, Id.* at page 4, line 8).

Claim 21

Claim 21 depends from claim 20 and indicates that the enzyme is selected from the group consisting of an oxidase, a peroxidase, a protease, a cell-wall lysing enzyme and a plaque matrix inhibitor. Claim 21 should be enabled for the same reasons as base claim 40 and since the as-filed specification discloses that the enzyme can be an oxidase, a peroxidase, a protease, a cell-wall lysing enzyme, or a plaque matrix inhibitor. (*See*, *Id.* at page 4, line 35 through page 5, line 5).

Claim 22

Claim 22 depends from claim 21 and indicates that the enzyme comprises an oxidase selected from the group consisting of glucose oxidase, lactase oxidase and uric acid oxidase. Claim 22 should be enabled for the same reasons as base claim 40 and since the as-filed specification teaches that the enzyme can be an oxidase such as glucose oxidase, lactase oxidase or uric acid oxidase. (*See*, *Id.* at page 4, lines 36-38).

Claim 24

Claim 24 depends from claim 21 and indicates that the enzyme comprises the protease and is selected from the group consisting of papain, pepsin, trypsin, ficin and bromelin. Claim 24 should be enabled for the same reasons as base claim 40 and since the as-filed specification discloses the enzyme can be a protease such as papain, pepsin, trypsin, ficin or bromelin. (*See*, *Id.* at page 5, lines 2-3).

Claim 27

Claim 27 depends from claim 2 and indicates that the diagnostically, therapeutically or cosmetically active substance comprises a fluorescent or radioactive substance. Claim 27 should be enabled for the same reasons as base claim 40 and since the as-filed specification describes that a fluorescent or radioactive substance can be coupled to the selected monoclonal antibody or fragment thereof. (*See*, *Id.* at page 4, line 7).

Claim 28

Claim 28 depends from claim 2 and indicates that the selected monoclonal antibody or fragment thereof is capable of binding an epitope of a pathogenic micro-organism or other pathogenic compound. Claim 28 should be enabled for the same reasons as base claim 40 and since the as-filed specification discloses that the selected monoclonal antibody or fragment thereof may be brought into contact with pathogens of the oral microflora. (*See*, *Id.* at page 4, lines 24-25).

Claim 29

Claim 29 depends from claim 28 and indicates that the pathogenic micro-organism is selected from the group consisting of Actinomyces actinomycetem comitans, Porphyromonas gingivalis, Prevotella intermedia, Streptococcus mutans, Bacteroides forsythus, Eikenella corrodens, Treponema denticola, Campylobacter lectus, and Fusobacterium nucleatum. Claim 29 should be enabled for the same reasons as base claim 40 since the as-filed specification discloses that the oral microflora includes the pathogens Actinomyces actinomycetem comitans, Porphyromonas gingivalis, Prevotella intermedia, Streptococcus mutans, Bacteroides forsythus, Eikenella corrodens, Treponema denticola, Campylobacter lectus, and Fusobacterium nucleatum. (*See*, *Id.* at page 4, lines 24-29).

Claim 30

Claim 30 is directed towards a composition comprising at least one selected monoclonal antibody or fragment thereof of claim 40 and at least one physiologically acceptable diluent, solvent or carrier. Claim 30 should be enabled for the same reasons as base claim 40 and since the as-filed specification discloses a composition including the at least one selected monoclonal antibody and at least one physiologically acceptable diluent, solvent or carrier. (*See*, *Id.* at page 17, claim 30).

Claim 31

Claim 31 depends from claim 30 and indicates that the composition is selected from the group consisting of a teeth cleaning agent, mouthwash, mouth spray, chewing tablet, chewing

gum, cream and ointment. Claim 31 should be enabled for the same reasons as base claim 40 and since the as-filed specification discloses that a medication including the selected monoclonal antibody or fragment thereof can take the form of a mouthwash, a lozenge or chewing tablet, a teeth cleaning agent, cream ointment or chewing gum. (*See, Id.* at page 5, lines 14-17).

Claim 35

Claim 35 depends from claim 10 and indicates that the first ion strength is 1 M NaCl and the second ion strength is 0 M. Claim 35 should be enabled for the same reasons as base claim 40 and since the as-filed specification discloses a working example of a selected monoclonal antibody or fragment thereof having the binding characteristics recited in claim 35. (*See, Id.* at page 7, Table 1).

Claim 42

Independent claim 42 is directed to a selected monoclonal antibody, or fragment thereof, that has been selected for its ability to bind an epitope at a first pH of 8.5 and such that the bond of the selected monoclonal antibody, or fragment thereof, to the epitope is broken at a second pH of 4.5 and an ion strength of 1M NaCl.

Claim 42 should be enabled since the as-filed specification discloses multiple working examples (*e.g.*, clones 47, 51, 5, 14 and 3 were shown to satisfy the conditions of selection D) of the selected monoclonal antibody or fragment thereof having the binding characteristics as recited in claim 42 at Tables 1 and 4. Thus, one of ordinary skill in the art would be able to make and use the selected monoclonal antibody or fragment thereof of claim 42 without undue experimentation. (*See, Id.* at pages 7 and 11).

Accordingly, claims 2, 9, 10, 13-22, 24, 27-31, 35, 40 and 42-49 should be enabled under 35 U.S.C. § 112, first paragraph, for the foregoing reasons.

Rejections under 35 U.S.C. § 103

35 U.S.C. § 103 Rejections of Claims 2, 9, 10, 13-22, 28, 30-31, 35, 40 and 42-49

Claims 2, 9, 10, 13-22, 28, 30-31, 35, 40 and 42-49

Claims 2, 9, 10, 13-22, 28, 30-31, 35, 40 and 42-49 stand rejected under 35 U.S.C. § 103(a) as assertedly being unpatentable over Beggs et al. in view of Goding.

The Final Office Action asserted that Beggs et al. teaches an antibody that is

> able to bind to a target site through antibody-antigen binding at conditions lie within physiologically acceptable limits ... pH of between 6 and 8 would be considered by one of ordinary skill in the art to lie within physiological limits ... Goding teaches that during optimization of each purification protocol for each antibody of interest and a fragment thereof, the parameters such as pH and ionic strength play an essential role and that it is an inherent properties [sic] of all antibody and fragment to bind to an epitope under one set of specifically chosen conditions and be eluted from an epitope ... under specifically chosen different conditions.

(Final Office Action at pages 5-6; *see also*, Advisory Action at page 4) (emphasis added). Thus, the Examiner is relying on the doctrine of inherency to formulate the obviousness rejections.

However, "[t]hat which may be inherent is not necessarily known. Obviousness cannot be predicated on what is unknown." (*In re Rijckaert*, 9 F3d 1531, 1534, 28 USPQ 2d 1955, (Fed. Cir. 1993), *citing In re Spormann*, 53 C.C.P.A. 1375, 363 F2d 444, 448, 150 USPQ 449, 452 (CCPA 1966)). Further, "[t]he fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic." (M.P.E.P. § 2112, *citing In re Rijckaert*, 9 F.3d at 1534, 28 USPQ 2d at 1957 (emphasis in original)). "To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference.'" (*Id.*, *citing In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999)). Thus, the examiner is improperly relying on the theory of inherency in concluding that all antibody and fragments thereof are eluted from an epitope at different conditions since no teaching, suggestion or motivation exists in Beggs et al. alone or in combination with Goding to indicate that antibodies bind or elute at the conditions of any of claims 2, 9, 10, 13-22, 28, 30-31, 35, 40 and 42-49.

Claim 40

A *prima facie* case of obviousness cannot be established with regard to independent claim 40 since the cited references do not alone or in combination teach or suggest each and every element of claim 40.

Claim 40 recites that the selected monoclonal antibody, or fragment thereof, binds to an epitope at a first pH of **8.5**. The Final Office Action asserts that "Beggs et al, teach an antibody and antibody fragment ... that are able to bind to a target site through antibody-antigen binding at conditions lie within physiologically acceptable limits ... pH of between 6 and 8 would be considered by one of ordinary skill in the art to lie within physiological limits." (Final Office Action at page 5) (emphasis added). However, a binding pH of **8.5** as recited in claim 40 does not fall within the physiologically acceptable limits (*i.e.*, pH of between 6 and 8) of Beggs et al. Also, Goding does not teach or suggest any selected monoclonal antibody or fragment thereof that binds at a pH of 8.5. Thus, Beggs et al. cannot alone or in combination with Goding teach or suggest each and every element of claim 40 as required to establish a *prima facie* case of obviousness.

Further, the cited references do not alone, or in combination, teach or suggest an antibody, or fragment thereof, having a bond between the antibody, or fragment thereof, and epitope broken at a pH of 7 as recited in claim 40. In formulating the obviousness rejection, the Final Office Action indicated that "it would have been obvious to one of ordinary skill in the art at the time the invention was made to determine all operable and optimal range[]s of pH and ion strength at which antibody of fragment thereof binds to and eluted from an epitope, and taught by Goding and use it for the antibody or fragment thereof of Beggs et al." (Final Office Action at page 6). However, the examiner has not indicated where Beggs et al. or Goding alone, or in combination, teach or suggest any antibody that dissociates at a pH of 7.

Further, during the interview of September 7, 2004, the examiner reasoned that in view of the Goding reference, which indicates that all antibodies inherently disassociate from their epitope at some condition, it is **possible** that the antibodies of Beggs et al. would disassociate at a pH of 7. However, even if inherency could be used to established obviousness, the examiner has not met the standard of the theory of inherency. As stated by the Federal Circuit

> to establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is **necessarily present** in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, **may not be established by probabilities or possibilities**. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.

(MPEP § 2112, *quoting In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999) (emphasis added)).

Further, the United States Supreme Court has stated that "[i]f the [claimed invention was] accidentally and unwittingly produced, whilst the operators were in pursuit of other and different results, ... without its even being known what was done or how it had been done, it would be absurd to say that this was an anticipation of [the present invention]." (*Tilghman v. Proctor*, 261 U.S. 707, 711-712 (1980)).[1]

However, since the Goding reference does not refer to the antibodies of Beggs et al., the cited references cannot establish that the antibodies of Beggs et al. **necessarily** disassociate at a pH of 7.

Further, to establish a *prima facie* case of obviousness, there must be a **reasonable expectation** of success. (*See*, MPEP § 2141, page 2100-120). However, the rationale asserted by the examiner that the antibody of Beggs et al. will bind at a pH of 6-8 and disassociate at a pH of 7 as assertedly taught by Goding is not supported by the references. Further, one of ordinary skill in the art would not expect an antibody that binds at a pH of between 6 and 8 to also dissociate at a pH of 7. For instance, the Goding reference, on which the examiner relies, indicates that in the majority of the cases, it is expected that harsh conditions will be required for the elution of antigen. (*See*, Goding, page 231). Thus, one of ordinary skill in the art would not reasonably expect the antibodies of Beggs et al., which bind at physiological conditions (which the examiner indicates are a pH of 6-8), to dissociate at a pH of about 7 (*i.e.*, within the

[1] Furthermore, inherency must be recognized by a person of ordinary skill in the art, (*see, Cont'l Can Co. USA v. Monsanto Co.*, 20 USPQ.2d 1746, 1749-1750 (Fed. Cir. 1991)), which states "[t]o serve as an anticipation when the reference is silent about the asserted inherent characteristic, such gap in the reference may be filled with recourse to extrinsic evidence. Such evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill."

physiological conditions) as recited in claim 40. An elution pH of 7 is not much harsher than a pH of 6-8. Thus, no reasonable expectation of success exists in assuming that the antibodies of Beggs et al. would dissociate at a pH of 7 as recited in claim 40.

The examiner also reasoned in the Advisory Action that "the parameters such as pH and ionic strength play an essential role and that it is an inherent properties of all antibody and fragment to bind to an epitope under one set of specifically chosen conditions and be eluted from an epitope (bound of antibody to an epitope is broken) under specifically chosen different conditions." (Advisory Action at page 4). However, there is nothing in the Beggs et al. or Goding et al. that indicates any of the disclosed monoclonal antibodies disassociate at a pH of 7 as recited in claim 40. Thus, the cited references do not establish that the antibodies of Beggs et al. **necessarily** disassociate a pH of 7 as asserted by the examiner.

Accordingly, a *prima facie* case of obviousness cannot be established for claim 40.

Since dependent claims 2, 9, 10, 13-22, 28, 30-31, 35, and 43-44 include the elements of independent claim 40, and a *prima facie* case of obviousness cannot be established with regard to claim 40, a *prima facie* case of obviousness also cannot be established with regard to any of dependent claims 2, 9, 10, 13-22, 28, 30-31, 35, and 43-44.

Claim 43

Claim 43 further defines the subject matter of claim 40. Thus, claim 43 is patentably distinct from claim 40 and the other claims.

A *prima facie* case of obviousness cannot be established with regard to claim 43 for at least the same reasons as base claim 40 and since the examiner has not indicated where Beggs et al. alone, or in combination with Goding, teaches or suggests a selected monoclonal antibody or fragment thereof that binds to an epitope of a *Staphylococcus epidermidis* origin as recited in claim 43.

Claim 16

Claim 16 further defines the subject matter of claim 15. Thus, claim 16 is patentably distinct from claim 14 and the other claims.

A *prima facie* case of obviousness cannot be established with regard to claim 16 for at least the same reasons as base claim 40 and since the examiner has not indicated where Beggs et al. alone, or in combination with Goding, teaches or suggests a selected monoclonal antibody or fragment thereof that is capable of bleaching teeth or molars included in the oral cavity as recited in claim 16.

Claim 24

Claim 24 further defines the subject matter of claim 21. Thus, claim 24 is patentably distinct from claim 21 and the other claims.

A *prima facie* case of obviousness cannot be established with regard to claim 24 for at least the same reasons as base claim 40 and since the examiner has not indicated where Beggs et al. alone, or in combination with Goding, teaches or suggests papain, pepsin, trypsin, ficin or bromelin as recited in claim 24.

Claim 26

Claim 26 further defines the subject matter of claim 21. Thus, claim 26 is patentably distinct from claim 21 and the other claims.

A *prima facie* case of obviousness cannot be established with regard to claim 2 for at least the same reasons as base claim 40 and since the examiner has not indicated where Beggs et al. alone, or in combination with Goding, teaches or suggests dextranase or mutanase as recited in claim 26.

Claim 27

Claim 27 further defines the subject matter of claim 2. Thus, claim 27 is patentably distinct from claim 2 and the other claims.

A *prima facie* case of obviousness cannot be established with regard to claim 27 for at least the same reasons as base claim 40 and since the examiner has not indicated where Beggs et al. alone, or in combination with Goding, teaches or suggests a fluorescent or radioactive substance as recited in claim 27.

Claim 28

Claim 28 further defines the subject matter of claim 2. Thus, claim 2 is patentably distinct from claim 2 and the other claims.

A *prima facie* case of obviousness cannot be established with regard to claim 28 for at least the same reasons as base claim 40 and since the examiner has not indicated where Beggs et al. alone, or in combination with Goding, teaches or suggests an epitope of a pathogenic micro-organism or other pathogenic compound as recited in claim 28.

Claim 29

Claim 29 further defines the subject matter of claim 28. Thus, claim 29 is patentably distinct from claim 28 and the other claims.

A *prima facie* case of obviousness cannot be established with regard to claim 29 for at least the same reasons as base claim 40 and since the examiner has not indicated where Beggs et al. alone, or in combination with Goding, teaches or suggests *Actinomyces actinomycetem comitans*, *Porphyromonas gingivalis*, *Prevotella intermedia*, *Streptococcus mutans*, *Bacteroides forsythus*, *Eikenella corrodens*, *Treponema denticola*, *Campylobacter lectus*, or *Fusobacterium nucleatum* as recited in claim 29.

Claim 42

A *prima facie* case of obviousness also cannot be established with regard to independent claim 42 since the cited references do not alone, or in combination, teach or suggest each and every element of claim 42.

Claim 42 recites that the selected monoclonal antibody or fragment thereof binds to an epitope at a first pH of **8.5**. The Final Office Action asserts that "Beggs et al, teach an antibody and antibody fragment ... that are able to bind to a target site through antibody-antigen binding at conditions lie within physiologically acceptable limits ... pH of between 6 and 8 would be considered by one of ordinary skill in the art to lie within physiological limits." (Final Office Action at page 5) (emphasis added). However, a binding pH of **8.5** as recited in claim 42 does not fall within the physiologically acceptable limits (*i.e.*, pH of between 6 and 8) of Beggs et al. Thus, Beggs cannot alone or in combination with Goding teach or suggest binding at a pH of 8.5

as recited in claim 42. Goding also does not teach or suggest any antibody that binds at a pH of 8.5. Accordingly, the cited references do not teach each and every element of claim 42 as required to establish a *prima facie* case of obviousness.

Further, the cited references do not alone, or in combination, teach or suggest an antibody, or fragment thereof, having a bond between the antibody, or fragment thereof, and epitope broken at a pH of 4.5 and an ion strength of 1M NaCl as recited in claim 42. In formulating the obviousness rejection, the Final Office Action indicated that "it would have been obvious to one of ordinary skill in the art at the time the invention was made to determine all operable and optimal range[]s of pH and ion strength at which antibody of fragment thereof binds to and eluted from an epitope, and taught by Goding and use it for the antibody or fragment thereof of Beggs et al." (Final Office Action at page 6).

However, this rationale is at least a hindsight reconstruction of the Appellant's inventive subject matter of claim 42 since there is no express suggestion or motivation to modify the antibodies of Beggs et al. or combine the antibodies of Beggs et al. with Goding. The rationale that

> [i]t would have been obvious to one of ordinary skill in the art at the time the invention was made to determine all operable and optimal rangers of pH and ion strength at which antibody or fragment thereof binds to and eluted from an epitope, as taught by Goding and use it for the antibody or fragment thereof taught by Beggs et al. (Advisory Action at page 4) (emphasis added)

appears to assume that the either the antibodies of Beggs et al. are modifiable or that the antibodies of Beggs et al. are combinable with the antibodies mentioned in Goding. However, claim 42 is not directed towards a method of **determining or selecting** all operable and optimal ranges of pH and ion strength at which an antibody or fragment thereof binds to and is eluted from an epitope as asserted in the Advisory Action. Rather, claim 42 is directed towards a **selected monoclonal antibody or fragment thereof** having specific binding characteristics which are not disclosed in Beggs et al. alone or in combination with Goding.

Further, as stated in the MPEP a "statement that modifications of the prior art to meet the claimed invention would have been "'well within the ordinary skill of the art at the time the claimed invention was made'" because the cited references relied upon teach that all aspects of the claimed invention were individually known in the art is not sufficient to establish a *prima*

facie case of obviousness." (MPEP § 2143.01, page 2100-131) (emphasis in original). Thus, the examiner cannot rely on the ordinary skill in the art without a teaching or suggestion to modify the references.

Accordingly, a *prima facie* case of obviousness cannot be established for claim 42.

35 U.S.C. § 103 Rejections of Claims 2, 9, 10, 13-21, 24, 27, 28, 30, 31, 35, 40 and 42-49

Claims 2, 9, 10, 13-21, 24, 27, 28, 30, 31, 35, 40 and 42-49

Claims 2, 9, 10, 13-21, 24, 27, 28, 30, 31, 35, 40 and 42-49 stand rejected under 35 U.S.C. § 103(a) as assertedly being unpatentable over Cummins et al. in view of Goding.

In formulating the obviousness rejections of claims 2, 9, 10, 13-21, 24, 27, 28, 30, 31, 35, 40 and 42-49, it was asserted that "it is an inherent properties of all antibody and fragment to bind to an epitope under one set of specifically chosen conditions and be eluted from an epitope ... under specifically chosen different conditions." (Advisory Action at page 3). However, as previously established herein, the theory of inherency cannot be used to formulate an obviousness rejection. (*See, In re Rijckaert, supra*; *see also*, M.P.E.P. § 2112, *supra*). Further, Cummins et al. does not alone or in combination with Goding teach or suggest each and every element of any of claims 2, 9, 10, 13-21, 24, 27, 28, 30, 31, 35, 40 and 42-49 as required for obviousness.

Claim 40

A *prima facie* case of obviousness cannot be established since Cummins et al. does not alone, or in combination with Goding, teach or suggest each and every element of claim 40. Claim 40 is directed to a selected monoclonal antibody, or fragment thereof, that has been selected for its ability to bind to an epitope at a first pH of 8.5 and such that the bond of the selected monoclonal antibody, or fragment thereof, to the epitope is broken at a second pH of 7.

The examiner indicated that "Cummins et al. teach various binding conditions that lie within physiologically acceptable limits, including pH and ion strength ... pH of between 6 and 8 would be considered by one of ordinary skill in the art to lie within physiological limits." (Final Office Action at page 7). However, independent claim 40 recites a binding condition of a first pH of **8.5** which does not fall within the binding conditions of Cummins et al. (*i.e.*, between 6

and 8) as stated in the Final Office Action. Further, Cummins et al. does not teach or suggest disassociation of the monoclonal antibody or fragment thereof from an epitope at a pH of 7 as recited in claim 40, and Goding does not teach or suggest any antibody that binds to an epitope at a pH of 8.5 and that disassociates at a pH of 7. Thus, the cited references do not teach each and every element of claim 40 as required to establish a *prima facie* case of obviousness.

A *prima facie* case of obviousness also cannot be established since no reasonable expectation exists in combining the cited references. For instance, one of ordinary skill in the art would not have a reasonable expectation of success in assuming that the antibodies of Cummins et al. would dissociate at a pH of 7 as recited in claim 40 in view of Goding. The Goding reference, on which the Office is relying, indicates that in the majority of cases it may be expected that harsh conditions for elution of antigen will be required. (*See*, Goding, page 231). Thus, the antibodies of Cummins et al. that bind at physiological conditions (which the Final Office Action indicates are a pH of 6-8) would not be expected to dissociate at a pH of about 7 as recited in claim 40 since Goding indicates that in the **majority** of cases, it is **expected** that much harsher conditions are required to elute an antibody from its antigen. Since a pH of 7 is not much harsher than a pH of 6-8, no reasonable expectation of success exists in order to establish a *prima facie* case of obviousness.

The Final Office Action also alleged that "it would have been obvious to one of ordinary skill in the art at the time the invention was made to determine all operable and optimal range[]s of pH and ion strength at which antibody or fragment thereof binds to and eluted from an epitope, as taught by Goding and use it for antibody or fragment thereof taught by Cummins et al." (*Id.*). However, claim 40 is not directed towards **determining or selecting** all operable and optimal ranges of pH and ion strength, but rather is directed towards a selected **monoclonal antibody or fragment thereof** having specific binding characteristics.

Further, in formulating the obviousness rejection of claim 40, the examiner is not viewing Cummins et al. as a whole. (*See*, M.P.E.P. § 2141.01). Rather, the examiner is merely focusing on the **binding properties** of the antibody of Cummins et al. If anything, when the Cummins et al. reference is viewed as a whole, one of ordinary skill in the art would conclude that Cummins et al. actually teaches away from eluting the antibody at a pH of 7 as asserted by

the examiner. The antibodies of Cummins et al. "are substantive (*i.e.*, withstand the flow of saliva), are not inhibited by soluble salivary components and remain reactive vs. their target in the presence of a developing biofilm." (Cummins et al., page 3, lines 30-31). Thus, when the antibodies of Cummins et al. are viewed as a whole, it is apparent that the antibodies are not designed to release from the epitope at physiological acceptable conditions, such as around pH 7, but rather that the antibodies of Cummins et al. are selected to bind substantively at physiological conditions.

Accordingly, a *prima facie* case of obviousness cannot be established for claim 40.

Since dependent claims 2, 9, 10, 13-21, 24, 27, 28, 30, 31, 35, and 43-44 include the elements of independent claim 40, and a *prima facie* case of obviousness cannot be established with regard to claim 40, a *prima facie* case of obviousness also cannot be established with regard to any of dependent claims 2, 9, 10, 13-21, 24, 27, 28, 30, 31, 35, and 43-44.

Claim 43

Claim 43 further defines the subject matter of claim 40. Thus, claim 43 is patentably distinct from claim 40 and the other claims.

A *prima facie* case of obviousness cannot be established with regard to claim 43 for at least the same reasons as base claim 40 and since the examiner has not indicated where Cummins et al. alone, or in combination with Goding, teaches or suggests a selected monoclonal antibody or fragment thereof that binds to an epitope of a *Staphylococcus epidermidis* origin as recited in claim 43.

Claim 19

Claim 19 further defines the subject matter of claim 14. Thus, claim 19 is patentably distinct from claim 14 and the other claims.

A *prima facie* case of obviousness cannot be established with regard to claim 19 for at least the same reasons as base claim 40 and since the examiner has not indicated where Cummins et al. alone, or in combination with Goding, teaches or suggests a targeted or temporary diagnostic, therapeutic or cosmetic treatment that comprises a treatment for fighting infections in externally accessible parts of the human or the animal body as recited in claim 19.

Claim 27

Claim 27 further defines the subject matter of claim 2. Thus, claim 27 is patentably distinct from claim 2 and the other claims.

A *prima facie* case of obviousness cannot be established with regard to claim 27 for at least the same reasons as base claim 40 and since the examiner has not indicated where Cummins et al. alone, or in combination with Goding, teaches or suggests a fluorescent or radioactive substance as recited in claim 27.

Claim 28

Claim 28 further defines the subject matter of claim 2. Thus, claim 28 is patentably distinct from claim 2 and the other claims.

A *prima facie* case of obviousness cannot be established with regard to claim 28 for at least the same reasons as base claim 40 and since the examiner has not indicated where Cummins et al. alone, or in combination with Goding, teaches or suggests an epitope of a pathogenic micro-organism or other pathogenic compound as recited in claim 28.

Claim 29

Claim 29 further defines the subject matter of claim 28. Thus, claim 29 is patentably distinct from claim 28 and the other claims.

A *prima facie* case of obviousness cannot be established with regard to claim 29 for at least the same reasons as base claim 40 and since the examiner has not indicated where Cummins et al. alone, or in combination with Goding, teaches or suggests *Actinomyces actinomycetem comitans*, *Porphyromonas gingivalis*, *Prevotella intermedia*, *Streptococcus mutans*, *Bacteroides forsythus*, *Eikenella corrodens*, *Treponema denticola*, *Campylobacter lectus*, or *Fusobacterium nucleatum* as recited in claim 29.

Claim 35

Claim 35 further defines the subject matter of claim 10. Thus, claim 35 is patentably distinct from claim 10 and the other claims.

A *prima facie* case of obviousness cannot be established with regard to claim 35 for at least the same reasons as base claim 40 and since the examiner has not indicated where Cummins et al. alone, or in combination with Goding, teaches or suggests a first ion strength of 1M NaCl and a second ion strength of 0M as recited in claim 35.

Claim 42

Independent claim 42 cannot be rendered obvious since Cummins et al. and Goding do not alone, or in combination, teach or suggest each and every element of claim 42. Claim 42 is directed to a selected monoclonal antibody or fragment thereof that has been selected for its ability to bind an epitope at a first pH of 8.5 and such that the bond of the selected monoclonal antibody or fragment thereof to the epitope is broken at a second pH of 4.5 and an ion strength of 1M NaCl.

As previously established herein, Cummins et al. is limited to binding of an antibody at physiological pH that the examiner indicates is a pH of 6-8. (*See*, Final Office Action at page 5). Since claim 42 recites a binding pH of **8.5**, Cummins et al. does not alone, or in combination with Goding, teach or suggest a binding pH of 8.5. Further, the Cummins et al. and Goding references do not alone, or in combination, teach or suggest disassociation conditions at a second pH of 4.5 and an ion strength of 1M NaCl as recited in claim 42.

The Final Office Action asserted "it would have been obvious to one of ordinary skill in the art at the time the invention was made to determine all operable and optimal range[]s of pH and ion strength at which antibody of fragment thereof binds to and eluted from an epitope, and taught by Goding and use it for the antibody or fragment thereof taught by, Cummins et al." (Final Office Action, page 6). However, as stated in the MPEP a "statement that modifications of the prior art to meet the claimed invention would have been "'well within the ordinary skill of the art at the time the claimed invention was made'" because the references relied upon teach that all aspects of the claimed invention were individually known in the art is not sufficient to establish a prima facie case of obviousness." (MPEP § 2143.01, page 2100-131) (emphasis in original). Since the examiner is relying on the ordinary skill of the art and **not** an express teaching or suggestion, a *prima facie* case of obviousness cannot be established for claim 42.

Further, as previously established herein, inherency cannot be used to establish obviousness. (*See, In re Rijckaert, supra*; *see also*, M.P.E.P. § 2112, supra). Thus, claim 42 is not obvious.

For all the foregoing reasons, claims 2, 9, 10, 13-21, 24, 27, 28, 30, 31, 35, 40 and 42-49 are not obvious in view of Beggs et al. and Goding.

35 U.S.C. § 103 Rejection of Claim 29

Claim 29

Claim 29 stands rejected under 35 U.S.C. § 103(a) as assertedly being unpatentable over Beggs et al. in view of Goding, and further in view of Cole et al.

Since dependent claim 29 includes the elements of independent claim 40, and a *prima facie* case of obviousness cannot be established with regard to claim 40, a *prima facie* case of obviousness also cannot be established with regard to dependent claim 29.

A *prima facie* case of obviousness also cannot be established with regard to claim 29 since the cited references do not alone, or in combination, teach or suggest each and every element of claim 29. Claim 29 depends from claim 28 and, thus, recites that the selected monoclonal antibody or fragment thereof binds to an epitope of *Porphyromonas gingavalis*. However, neither Beggs et al. nor Goding teach, suggest or motivate a monoclonal antibody or fragment thereof that binds to *Porphyromonas gingavalis*, and Cole et al. does not teach, suggest or motivate the presence of any monoclonal antibody or fragment thereof.

Cole et al. is limited to a study for the presence of IgM and IgG antibodies in serum of peridontally healthy children and subjects with localized juvenile periodontitis. (*See*, Cole et al., page 33). In fact, the only relevance of Cole et al. appears to be that the term *Porphyromonas gingavalis* is mentioned. Thus, Cole et al. does not teach or suggest, and is not concerned with the use of or selection of any monoclonal antibody or fragment thereof. Accordingly, a *prima facie* case of obviousness cannot be established with regard to claim 29.

35 U.S.C. § 103 Rejection of Claim 43

Claim 43

Claim 43 stands rejected under 35 U.S.C. § 103(a) as assertedly being unpatentable over Beggs et al. in view of Goding, and further in view of Fischer.

Since dependent claim 43 includes the elements of independent claim 40, and a *prima facie* case of obviousness cannot be established with regard to claim 40, a *prima facie* case of obviousness also cannot be established with regard to dependent claim 43.

A *prima facie* case of obviousness also cannot be established since the cited references do not alone, or in combination, teach or suggest each and every element of claim 43. Claim 43 depends from claim 40 and further recites that the selected monoclonal antibody or fragment thereof binds to an epitope of a *Staphylococcus epidermidis* origin, wherein the monoclonal antibody or fragment thereof binds to the epitope of *Staphylococcus epidermidis* origin under the conditions of claim 40. However, as previously established herein, neither Beggs et al. nor Goding teach, suggest or motivate a selected monoclonal antibody or fragment thereof that binds the epitope of a *Staphylococcus epidermidis* origin, and Fischer does not teach, suggest or motivate a selected monoclonal antibody or fragment thereof that possesses the binding characteristics recited in claim 40.

Fischer merely indicates that antibodies or monoclonal antibodies exist that bind *Staphylococcus epidermidis*. (*See generally*, Fischer). Fischer does not teach, suggest or motivate the specific binding conditions as recited in claim 40. Thus, the cited references cannot establish a *prima facie* case of obviousness for claim 43.

CONCLUSION

Appellants request the reversal of the rejections of currently pending claims 2, 9-10, 13-22, 24, 27-31, 35, 40 and 42-49 for the foregoing reasons.

Respectfully submitted,

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Date: March 10, 2005
AFN

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CLAIMS APPENDIX

1. (Canceled).

2. (Previously presented) The selected monoclonal antibody, or fragment thereof, of claim 40, wherein the selected monoclonal antibody, or fragment thereof, is coupled to a diagnostically, therapeutically or cosmetically active substance.

3-8. (Canceled).

9. (Previously presented) The selected monoclonal antibody, or fragment thereof, of claim 40, wherein the ability of the selected monoclonal antibody, or fragment thereof, to bind to the epitope has been further selected dependent upon ion strength.

10. (Previously presented) The selected monoclonal antibody, or fragment thereof, of claim 9, wherein:

a first ion strength at which the selected monoclonal antibody binds the epitope is different than a second ion strength at which the bond between the selected monoclonal antibody and the epitope is broken.

11-12. (Canceled).

13. (Previously presented) The selected monoclonal antibody, or fragment thereof, of claim 40, wherein the selected monoclonal antibody, or fragment thereof, is selected from a group consisting of a F(ab), F(ab)', $F(ab)'_2$ and an scFv.

14. (Previously presented) The selected monoclonal antibody, or fragment thereof, of claim 40, wherein the selected monoclonal antibody, or fragment thereof, is capable of use in a targeted or temporary diagnostic, therapeutic and cosmetic treatment of externally accessible parts of the human or the animal body.

15. (Previously presented) The selected monoclonal antibody, or fragment thereof, of claim 14, wherein said targeted or temporary diagnostic, therapeutic or cosmetic treatment comprises a treatment of an oral cavity of the human or the animal body.

16. (Previously presented) The selected monoclonal antibody, or fragment thereof, of claim 15, wherein the selected monoclonal antibody, or fragment thereof, is capable of bleaching teeth and molars included in said oral cavity.

17. (Previously presented) The selected monoclonal antibody, or fragment thereof, of claim 15, wherein the selected monoclonal antibody, or fragment thereof, is capable of detecting plaque in said oral cavity.

18. (Previously presented) The selected monoclonal antibody, or fragment thereof, of claim 15, wherein the selected monoclonal antibody, or fragment thereof, is capable of removing plaque in said oral cavity.

19. (Previously presented) The selected monoclonal antibody, or fragment thereof, of claim 14, wherein said targeted or temporary diagnostic, therapeutic or cosmetic treatment comprises a treatment for fighting infections in externally accessible parts of the human or the animal body.

20. (Previously presented) The selected monoclonal antibody, or fragment thereof, of claim 2, wherein the diagnostically, therapeutically or cosmetically active substance comprises an enzyme.

21. (Previously presented) The selected monoclonal antibody, or fragment thereof, of claim 20, wherein the enzyme is selected from the group consisting of an oxidase, a peroxidase, a protease, a cell-wall lysing enzyme and a plaque matrix inhibitor.

22. (Previously presented) The selected monoclonal antibody, or fragment thereof, of claim 21, wherein the enzyme comprises an oxidase selected from the group consisting of glucose oxidase, lactase oxidase and uric acid oxidase.

23. (Withdrawn) The antibody, or fragment thereof, of claim 21, wherein the enzyme comprises an oxidase chosen from a group consisting of glucose oxidase, lactase oxidase and uric acid oxidase.

24. (Previously presented) The selected monoclonal antibody, or fragment thereof, of claim 21, wherein the enzyme comprises the protease and is selected from the group consisting of papain, pepsin, trypsin, ficin and bromelin.

25. (Withdrawn) The antibody, or fragment thereof, of claim 21, wherein the enzyme comprises lysozyme.

26. (Withdrawn) The antibody, or fragment thereof, of claim 21, wherein the enzyme comprises a plaque matrix inhibitor chosen from a group consisting of dextranase and mutanase.

27. (Previously presented) The selected monoclonal antibody, or fragment thereof of claim 2, wherein the diagnostically, therapeutically or cosmetically active substance comprises a fluorescent or radioactive substance.

28. (Previously presented) The selected monoclonal antibody, or fragment thereof, of claim 2, wherein the selected monoclonal antibody, or fragment thereof, is capable of binding an epitope of a pathogenic micro-organism or other pathogenic compound.

29. (Previously presented) The selected monoclonal antibody, or fragment thereof, of claim 28, wherein said pathogenic micro-organism is selected from the group consisting of Actinomyces actinomycetem comitans, Porphyromonas gingivalis, Prevotella intermedia, Streptococcus mutans, Bacteroides forsythus, Eikenella corrodens, Treponema denticola, Campylobacter lectus, and Fusobacterium nucleatum.

30. (Previously presented) A composition comprising:
at least one selected monoclonal antibody, or fragment thereof, of claim 40; and
at least one physiologically acceptable diluent, solvent or carrier.

31. (Previously presented) The composition of claim 30, wherein the composition is selected from the group consisting of a teeth cleaning agent, mouthwash, mouth spray, chewing tablet, chewing gum, cream and ointment.

32-34. (Canceled).

35. (Previously presented) The selected monoclonal antibody, or fragment thereof, of claim 10, wherein the first ion strength is 1 M NaCl and the second ion strength is 0 M.

36-39. (Canceled).

40. (Previously presented) A selected monoclonal antibody, or fragment thereof, wherein:
the selected monoclonal antibody, or fragment thereof, has been selected for its ability to bind to an epitope at a first pH of 8.5; and
the selected monoclonal antibody, or fragment thereof, has also been selected such that the bond of the selected monoclonal antibody, or fragment thereof, to the epitope is broken at a second pH of 7.

41. (Canceled).

42. (Previously presented) A selected monoclonal antibody, or fragment thereof, wherein:

the selected monoclonal antibody, or fragment thereof, has been selected for its ability to bind an epitope at a first pH of 8.5; and

the selected monoclonal antibody, or fragment thereof, has also been selected such that the bond of the selected monoclonal antibody, or fragment thereof, to the epitope is broken at a second pH of 4.5 and an ion strength of 1M NaCl.

43. (Previously presented) The selected monoclonal antibody, or fragment thereof, of claim 40, wherein the epitope is of a *Staphylococcus epidermidis* origin.

44. (Previously presented) The selected monoclonal antibody, or fragment thereof, of claim 40, wherein the first pH is about 8.5.

45. (Previously presented) The selected monoclonal antibody, or fragment thereof, of claim 42, wherein the first pH is about 8.5.

46. (Previously presented) The selected monoclonal antibody, or fragment thereof, of claim 42, wherein the second pH is about 4.5.

47. (Previously presented) The selected monoclonal antibody, or fragment thereof, of claim 45, wherein the second pH is about 4.5

48. (Previously presented) The selected monoclonal antibody, or fragment thereof, of claim 42, wherein the ability of the selected monoclonal antibody, or fragment thereof, to bind to the epitope has been further selected dependent upon ion strength.

49. (Previously presented) The selected monoclonal antibody, or fragment thereof, of claim 48, wherein the ion strength is equivalent to about 1M NaCl.

EVIDENCE APPENDIX

No additional evidence was submitted.

RELATED PROCEEDINGS APPENDIX

No relevant appeal or interference decisions are known to the appellants or the appellants' representatives.

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TRANSMITTAL FORM

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Examiner Name	M. Belyavskyi
Attorney Docket Number	2183-4753US

ENCLOSURES *(check all that apply)*

- ☒ Postcard receipt acknowledgment (attached to the front of this transmittal)
- ☒ Duplicate copy of this transmittal sheet in the event that additional filing fees are required under 37 C.F.R. § 1.16
- ☐ Preliminary Amendment
- ☐ Response to Restriction Requirement/Election of Species Requirement dated
- ☐ Amendment in response to office action dated
- ☐ Amendment under 37 C.F.R. § 1.116 in response to final office action dated
- ☐ Additional claims fee - Check No. in the amount of $
- ☐ Letter to Chief Draftsman and copy of FIGS. with changes made in red
- ☐ Transmittal of Formal Drawings
- ☐ Formal Drawings (sheets)
- ☐ Information Disclosure Statement, PTO/SB/08A; ☐ copy of cited references
- ☐ Supplemental Information Disclosure Statement; PTO/SB/08A; copy of cited references and Check No. in the amount of $180.00
- ☐ Associate Power of Attorney
- ☒ Petition for Extension of Time and Check No. in the amount of $60.00
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- ☐ Certified Copy of Priority Document(s)
- ☐ Assignment Papers *(for an Application)*
- ☐ Terminal Disclaimer
- ☐ Terminal Disclaimer
- ☐ Terminal Disclaimer
- ☒ Other Enclosure(s) *(please identify below)*:

  Appeal Brief (35 pages in triplicate)

Remarks

The Commissioner is authorized to charge any additional fees required but not submitted with any document or request requiring fee payment under 37 C.F.R. §§ 1.16 and 1.17 to Deposit Account 20-1469 during pendency of this application.

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm *or* Individual name	Andrew F. Nilles — Registration No. 47,825
Signature	Andrew F. Nilles
Date	March 10, 2005

CERTIFICATE OF MAILING

Express Mail Label Number: EL994844087US

Date of Deposit: March 10, 2005

Person Making Deposit: Steve Wong